

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicant** 

: Goddard et al. (as amended)

Appl. No.

10/036,342

Filed

: December 26, 2001

For

POLYPEPTIDES THAT INDUCE

CELL PROLIFERATION (as

amended)

Examiner

Kolker, Daniel E.

Group Art Unit

1649

## **DECLARATION UNDER 37 CFR §1.131**

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

## Dear Sir:

We declare and state as follows:

- 1. We are the inventors of the invention claimed in the above-captioned patent application.
- 2. During the time period in which we participated in the events and activities described herein, we were employed by Genentech, Inc., the assignee of the above-captioned application.
- 3. All of the events and activities described herein were performed by us personally, or by others at our direction as part of our duties as employees of Genentech, Inc.
- 4. The invention claimed in the above-captioned patent application was conceived and reduced to practice in the United States prior to November 10, 1999 as described below.
- 5. Prior to November 10, 1999, we conceived of the invention claimed in the above-captioned patent application. This is demonstrated by the attached sequence printout (Exhibit A), which was generated prior to November 10, 1999, and which shows the complete sequence of the nucleic acid having the sequence of SEQ ID NO: 56. The attached printout also shows the complete sequence of the polypeptide which has the sequence of SEQ ID NO: 57. As evidenced by the sequence printout, we were in possession of the complete nucleic acid and amino acid sequences prior to November 10, 1999.
- 6. The date deleted from Exhibit A is prior to November 10, 1999. This date was redacted pursuant to M.P.E.P. § 715.07. The date that remains is the date the report was printed, April 28, 2005.
- 7. After these initial experiments, we diligently reduced the claimed subject matter to practice by working to express and purify the encoded polypeptide and to run it systematically

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- 8. Exhibit B shows that the protein lot designated PIN1205-1 was delivered to James Pan on a date prior to November 10, 1999 in order to perform assay ASY92, called "Mouse Mesangial Cell proliferation Assay." Also, as shown in Exhibit B, the assay was completed on a date prior to November 10, 1999. Exhibit B also shows that the tested polypeptides tested positive ("All Positives"), thereby confirming the ability of the encoded polypeptide to induce mesangial cell proliferation. Thus, actual reduction to practice occurred on a date prior to November 10, 1999.
- 9. The dates deleted from Exhibit B all are prior to November 10, 1999. These dates were redacted pursuant to M.P.E.P. § 715.07. The date that remains is the date the report was printed, April 28, 2005.
- 10. After reducing the invention to practice, we worked with the Genentech, Inc. patent department to prepare a non-provisional patent application, which included the sequences of SEQ ID NO:56 and SEQ ID NO:57, as well as the data showing the ability to induce mesangial cell proliferation. That application was filed on March 1, 2000 as PCT/US00/05601.
- 11. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Bv:	J. Lodon	Date: 19 007 05
_, _	Audrey Goddard	
Ву: _		Date:
	Paul J. Godowski	•
By: _		Date:
	Austin L. Gurney	
By:		Date:
. –	James Pan	
Bv:		Date:
<b>,</b> -	Colin K. Watanabe	
By: _		Date:
	William I. Wood	

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By: _	· · · · · · · · · · · · · · · · · · ·	Date:
	Andrey Goddard  Paul J. Godowski	Date: 10/18/05
Ву: _	Austin L. Gurney	Date:
By: _	James Pan	Date:
Ву: _	Colin K. Watanabe	Date:
Ву: _	William I. Wood	Date:

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By:	Date:
Audrey Goddard	
By:Paul J. Godowski	Date:
By:Austin L. Gurney	Date:
By: James Pan	Date: 10/18/0 [
By: Colin K. Watanabe	Date:
By:William I. Wood	Date:

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By: _		Date:
	Audrey Goddard	
Ву: _	Paul J. Godowski	Date:
Ву: _	Austin L. Gurney	Date:
Ву: _	James Pan	Date: Oct 24/05
Ву: _	Colin K. Watanabe	Date:
By: _	William I. Wood	Date:

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By: _	AJ C111	Date:
•	Audrey Goddard	
Ву: _		Date:
	Paul J. Godowski	
Ву: _		Date:
	Austin L. Gurney	
By: _	·	_ Date:
	James Pan	
Ву: _	Coin K Watander	Date: Cot 20, 2005
	Colin K. Watanabe	,
By:		Date:
	William I. Wood	

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By: _		Date:
	Audrey Goddard	
By: _	Paul I Godovalei	Date:
	Paul J. Godowski	
By: _		Date:
	Austin L. Gurney	
Ву: _		Date:
	James Pan	
By: _	Calla V. War.	Date:
•	Colin K. Watanabe	
Ву: _	William & Wood	Date: 10/16/05
	William I. Wood	

EXHIBIT A

[DNA92234], sheldens >Sequence confirmed by phredphrap >Thursday, April 28, 2005 >887 Sites [All Sites] >DNA92234 [Full] > 1.1b309

thai

mnll taqI fnuDII/mvnI snaBI nlaIII sphī

nepHI bstUI tail

xhoI **bsh1236I** tail nspl

tsp5091[M.ecoRI-] maeli/hpyCH4IV bsiWi/spli

tiii smlI ecoRI hpy1881 hinlI/acyl cac8I bsaAl ahall/bsaHl mlul rsal aluI

tsp45I

maeIII

paeR7I aatii cac8i afiiii maeii/hpyCH4IV mboII. sapī

bpmI/g

hpy1881 acil

muli

fnu4HI/bsoFI hpy18 1 INGENGACAC ININGANGNG CINIGACGIC GCAIGCACGC GIACGIAAGC ICGGAAITCG GCICGAGGAA IGAAIACCIC CGAAGCCGCI IIGITCICCA aval[M.taqI-] hphl sfcI earl/ksp6321 hpy991 hpyCH4V csp61 alul apol

ATOCACTOTG ATAICTICIC GATACTGCAG COTACGTGCG CATGCATTCG AGCCTTAAGC CGAGCTCCTI ACTTATGGAG GCTTCGGCGA AACAAGAGGT

Ansert starts here

scrFI[M.hpail-]

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bpuAI

bsp1286

DmyI

tru9I hphi

101 GAIGTGAATA GCICCACTAT ACCAGCCICG ICTTCCTICC GGGGGACAAC GIGGGICAGG GCACAGAGAG AIAITTAAIG ICACCCICTI GGGCTTICA msel maeili maeII/hpyCH4IV mnll mboll bsaJI

sau3AI

mpoI/ndeII[dam-]

dpnII[dam-]

dpnI[dam+]

alwI[dam-]

nlaIV

bstYI/xholI

mnll

bamHI bslI

fnu4HI/bso bbvI bsmFI

hgaI tseI

> hpy188III alw1[dam-] hpy188I batXI

201 TOGGACTOCC TOTGCCACAT TITITGGAGG TIGGGAAAGT TGCTAGAGGC TICAGAACTC CAGOCTAATG GATOCCAAAC TOGGGAGAAT GGOTGCGTOC eco57I bpmI/gsul[dcm-] bsll aval

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plei mlyI ACCCTGAGGG AGACGGTGTA AAAAACCICC AACCCTTTCA ACGATCTCCG AAGTCTTGAG GTCGGATTAC CTAGGGTTTG AGCCCTCTTA

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CCGACGCAGG

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GSeqEdit, DNA92234 [Full], page 2

Idem

hpaII

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bsmFI tail Ilsd Isdd

CTACACTTAT CGAGGTGATA TGGTCGGAGC AGAAGGAAG CCCCCTGTTG CACCCAGTCC CGTGTCTCTC TATAAATTAC AGTGGGAGAA CCCCGAAAGT

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tsel acii  tsel mwol thainlaili haeii  mwol fnu4HI/bsoFi fnuDII/mwni  bbvi bbvi bbvi bsh1236i mni hai/cfoi mni acii bssKi xmni mboli csp6i ecoNi  cac8i bbvi bbwi bpmi/gsu[[dcm-], bseRi mnii bsli bsaji hhai/cfoi asp700 bsri bsli  301 CTGCTGCTG GCTGCTGAG GCGGCATGT TCTCCTCAC CTCCCCCC CCGGCGCTGT TAGAGAAAGT CTTCCAGTAC ATTGACCTCC	•					ms	Н	ecoNI	H	႘
tsel acii  tsel mwol thainlaili haeli  mwol finu4Hi/bsoFi finuDii/mwol  bbvi bbvi bstUi[M.hhai-]  tsel tsel tsel bsh1236i dsaV hinPi bpuAi  mwol finu4Hi/bsoFi hinPi nspl hphi mwol hpali bsbii csp6i  cac8i bbvi bbwi bpmi/gsui[dcm-], bseRi mmli bsli bsaJi hhai/cfoi asp700 bsri  CTGCTGGCTG TGCTGCTG GCTGCTGAG CGCGGCATGT TAGAGARAAGT CTTCCAGTAG.							mn1		bsl	ATTGACCI
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tsel acti  tsel mwol thainlaili haeii  mwol fnu4HI/bsoFi fnuDII/mwni  bbvi bbvi bstUI[M.hhai-] acif[M.hpaii-]  tsel tsel bsh1236i hphi mwol hpaii  mwol fnu4HI/bsoFi hhai/cfoi mnli acii bssKi  cac81 bbvi bbwi bpmi/gsuI[dcm-], bseRi mnli bsli bsaJi hhai/cfoi asi  CTGCTGGCTG TGCTGCTG CCGGCGTT TGGARA		•	•			bpuAI	:Isqq	II mboII	3700 3	AGT CTTC
tsel acii  tsel mwol thainlaili haeli  mwol fnu4HI/bsoFi fnuDII/mwol  bbvi bbvi bstUI[M.hhai-] acif[M.hpaii  tsel tsel bsh1236i dsav hinpi  mwol fnu4HI/bsoFi hinpi nspi hphi mwol hpaii  mwol fnu4HI/bsoFi hhai/cfoi mnli acii bssKi  cac8i bbvi bbwi bpmi/gsuI[dcm-], bseRi mnli bsli bsaJi hhai/cfoi  CTGCTGGCTG TGCTGCTGGAG CGCGGCATGT TCTCCTCACC CTCCCCCCC CCGGCGCTGT 7				· •				X		AGAGAA
tsel acii  tsel mwol thainlaili  mwol fnu4HI/bsoFi nspHi fnu4HI/bsoFi fnuDII/mwni bbvi bbvi bstUI[M.hhai-]  tsel tsel bshl236i  mwol fnu4HI/bsoFi hinPi nspi hphi  mwol fnu4HI/bsoFi hhai/cfoi mnli  cac8i bbvi bbwi bpmi/gsu[dcm-]. bseRi mnl  CTGCTGGCTG TGCTGCTGGAG GGGGGATGT TCTCCTCACC		haeII	Idem	scrFI[M.hpaII-	ncil	dsav hinPI	mwol hpall	acil basKI	II balI bsaJI hhaI/cfoI	Trecesses essession I
tsel acil tsel mwol thal nlall] mwol fnu4HI/bsoFi nspHI fnu4HI/bsoFi fnuDII/mwnl bbvI bbvI bstUI[M.hha tsel tsel bstIl[M.hha tsel tsel bshl2361 mwol fnu4HI/bsoFI hinPI nspI mwol fnu4HI/bsoFI hhaI/cfoI cac81 bbvI bbvI bpmI/gsuI[dcm-]. CTGCTGGCTG TGCTGCTGCT GCTGCTGGT	•				I-]		hphI	mli	bseRI mm.	TCTCCTCACC (
tsel tsel mwol tsel mwol fnu4HI/bsoF bbvI bbvI bbvI bbvI tsel tsel mwol fnu4HI/b mwol fnu4HI/b cac8I bbvI bbvI CTGCTGGCTG TGCTGCTGCT			HI/bsoFI nspHI			bsh1236I	sofi hinpi nspi	hhaI/cfoI	bpmI/gsul[dcm-].	CTGGAG CGCGGCATGT
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GACGACCGAC ACGACGACGA CGACGACCTC GCGCCGTACA AGAGGAGTGG GAGGGGGGG GGCGCGACA ATCTCTTTCA GAAGGTCATG TAACTGGAGG

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						tth1111/aspI	pleI .

bsp1286[M.aluI-] bsiHKAI hpy188I

pflfi

haeIII/palI

mlyi · hinfi

eael taqI

mscI/ball

alwNI[dcm-] alw26I/bsmAI

foki tsp5091

apoI

прусн4у

batF5I

bmyl eco571

hpy188I

401 ATCAGGATGA ATTIGTGCAG ACGCTGAAGG AGTGGGTGGC CATCCAGAGC GACTCTGTCC AGCCTGTGCC TCGCTTCAGA CAAGAGCTCT TCAGAATGAT TAGICCIACT INANCACGIC JGCGACTICC JCACCCACCG GIAGCICICG CIGAGACAGG ICGGACACGG AGCGAAGICI GITCICGAGA AGICITACIA banII[M.aluI-] mnli eco571 hpy188III cfrI bsgI hgaI eco57I hpy188III

O E L F PVP D S V S 13 H W V A O D E

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						tseI	fnu4HI/bsoFI	aluI	pvuil[M.H1-]	tseI	fnu4HI/bsoFI	sau96I alwNI[dcm-]	ppuMI ddeI mspAll/nspBII	nlaIV bspCNI bbvI
scrFI[dcm-]	pspGI sau96I[M.haeIII-]	mvaI pspOMI/bsp120I	ecoRII[dcm-]	dsaV[dcm-]	bstNI nlaIV	baskI[dcm-]	hinPI bsp1286[M.haeIII-]	hhal/cfol sfil	JI bmyl	fnu4HI/bsoFI sau96I[M.haeIII-]	I[dcm+]	<pre>banII[M.haeIII-]</pre>	apal	tsel alwNI[dcm-] haeIII/palI bsaJI
367	isd	mva	900	dsa	bst	seq	hinPI	hhaI/c	tsel bsaJl bmyl	fnu4HI/bs	bbvI apyI[dcm+]	hpyCH4V	sfc, haell	tsel alwNi[dc
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I P D o o Σ Ω VASV G A R R E ADTL 79. A V A

501 GECCETGECT GCGGACACGC TGCAGCGCCT GGGGGCCCCGT GTGGCCTCGG TGGACATGGCA CTGCCCGATG GTCAGAGTCT TCCAATACCT COGGCACCGA CECCIGIGGG ACGICGCGGA CCCCGGGGCA CACCGGAGCC ACCIGIACCC AGGAGICGIC GACGGGCIAC CAGICICAGA AGGITAIGGA

bbvI alw261/bsmAI bgll[M.haeIII-]

eco01091/drall

fnu4HI/bsoFI

bceAl bbvI haeIII/palI

muli

hinfI

hpy188I

pshAI avaII alw26I/bsmAI

plei mlyI

nlaIV bspCNI bbvI ecool091/drall nlaili mnli bbvī

haeIII/palI

nlafV

mwol fnu4HI/bsoFI pst1[M.Hl-]

Tlodm bpuAI bbsI

eaeI[dcm-]

scrFI[dcm-] 19dsd

mvaI

ecoRII[dcm-]

fnu4HI/bsoFI mspI bsqI cac8I tseI haeIII/palI mbol/ndeII[dam-] bst4CI/hpyCH4III dralli IOWIII ball sau3AI bssKI [dcm-] dsaV[dcm-] bstNI bslI

scrFI[M.hpaII-]

nciI

eaeI bstAPI dpnII[dam-]

hpall basKI dsaV bsaJI maeII/hpyCH4IV btrI hpyCH4V tail bbvI cfrI bceAI IOM田 nlaIV banI dpnI[dam+] alw[[dam-] bstF51 haeIII/pall foki cfri bsri apyI[dcm+]

GGGCAGIAGE ACCGGCITGA COCCICGCIA GGGIGCITIC CGIGGCACAC GAAGAIGCCG GIGAACCIGC ACGIOGGACG ACTGGCCCCG CIACCCACCG . 601 cocricatoc tescogaact essaascat cocaceaas scaccetsts citétacses cactesacs tecasoctes teaccesses saissestes H >+ ນ > T .K .G S D A E L 112 P V I L

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701 TCACGGACCC CTATGTGCTG ACGGAGGTAG ACGGGAAACT TTATGGACGA GGAGCGACCG ACAACAAÁGG CCCTGTCTTG GCTTGGATCA ATGCTGTGAG AGTGCCTGGG GAIACACGAC TGCCTCCATC TGCCCTTTGA AATACCTGCT CCTCGCTGGC TGTTGTTTCC GGGACAGAAC CGAACCTAGT TACGACACTC I M. Y H N GATD بم ن > =

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						Ä	£	hpy18	co57I	rg H

801 CGCCTICAGA GCCCTGGAGC AAGATCTTCC TGTGAATATC AAATTCATCA TTGAGGGGAT GGAAGAGGCT GGCTCTGTTG CCCTGGAGGA ACTTGTGGAA GOGGAAGICT CGGGACCICG TICIAGAAGG ACACITATAG TITAAGIAGT AACICCCCIA CCITCICCGA CCGAGACAAC GGGACCICCT TGAACACCIT GSVA 전 표 표 **∑** 떮 KFII I N A D L ALEQ 179 A F R

mwoI banII bpmI/gsuI[dcm-]

bssKI bsaJI dsaV

xmaI/ps

smaI

scrřI [M

nctr

dsaV

bssKI

mbol/ndeII[dam-] dpnII[dam-] dpn[(dam+]

sau3AI

bsaJI

avaI[M.

901 AAAGAAAAG ACCGAITCIT CICTGGIGIG GACTACATIG TAAITICAGA TAACCIGIGG ATCAGCCAAA GGAAGCCAGC AATCACTIAI GGAACCCGGG cac8I alwI[dam-]

ITTCITITCC TGGCTAAGAA GAGACCACAC CTGATGTAAC ATTAAAGTCT ATTGGACACC TAGTCGGTTT CCTTCGGTCG TTAGTGAATA CCTTGGGCCC

hpy188Itsp509I

sau961 mboll avaII hinfI

scrFI[dcm-]

pspGI mval ecoRII[dcm-]

dsaV[dcm-]

bstNI

baskI[dcm-]

hpy188III

mbol/ndeII[da

sau3AI

nlaii

rcal

dpnII[dam-]

dpnI[dam+] ea

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fokī bsmAI

bstF5I hpy188III gfaNI ddeI nlaIV bspCNI hpyCE4V apyl[dcm+] bsaI

1001 GGAACAGCTA CITCATGGTG GAGGTGAAAT GCAGAGACCA GGATTITCAC TCAGGAACCT TTGGTGGCAI CCTTCATGAA CCAAIGGCTG AICTGGTTGC

nlaili mnli

CCITICICGAI GAAGIACCAC CICCACIIIA CGICICIGGI CCIAAAAGIG AGICCIIGGA AACCACCGIA GGAAGIACII GGIIACCGAC IAGACCAACG P M A D E E I. 9 9 S G T D F H R D Q

scrFI [dcm-] papGI ecoRII[dcm-]

mvaI

dsaV[dcm-] bstNI

bssKI [dcm-

sau96I[dcm-] nlarv

avaII[dcm-]

scrfi[dcm-]

scrfl[dcm-]

pspGI apyI[dcm+]

pspGI pleI

mval bsmFl

mvaI

ecoRII[dcm-] ecoRII[dcm-] mlyI

bstNI bsaJI dsaV[dcm-] bstNI hinfI dsaV[dcm-]

bssKI[dcm-] tffI

bssKI[dcm-]

apy1[dcm+]

xmil nlaIV

asp700

apy1[dcm+] hinfl

earI/ksp632I

mnlī mboII

1101 TCTTCTOGGT AGCCTGGTAG ACTCGTCTGG TCATATCCTG GTCCCTGGAA TCTATGATGA AGTGGTTCCT CTTACAGAAG AGGAAATAAA TACATACAAA

AGAAGAGCCA ICGGACCAIC IGAGCAGACC AGIAIAGGAC CAGGGACCIT AGAIACIACÍ ICACCAAGGA GAAIGICIIC ICCITIAITI AIGIAIGIII 回 取 日 V V SIV 279 L L G

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acc651 hpy188III

mli hpyCH4V ddeI bseRI hinfI mil téir taqī tsp509I

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1201 GCCATCCATC TAGACCTAGA AGAATACCGG AATAGCAGCC GGGTTGAGAA ATTTCTGTTC GATACTAAGG AGGAGATTCT AATGCACCTC TGGAGGTACC

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foki hpy188III mboli

bstFSI bfaI bfaI

maeI

xbaI

maeī rmaI

bbvI

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OGGTAGGTAG ATCTGGATCT TCTTATGGCC TTATCGTCGG CCCAACTCTT TAAAGACAAG CTATGATTCC TCCTCTAAGA TTACGTGGAG ACCTCCATGG

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.hinPI

mnll bstUI[M.hhaI-] mvaI

mbol/ndell[dam-][M.taql-]

dpnII[dam-] dpnI[dam+]

hhaI/cfoI

19dsd

mval

ecoRII[dcm-]

ecoRII[dcm-]

dsaV[dcm-] bstNI

bssKI [dcm-] dsaV[dcm-]

bstNI

apyI[dcm+] bssKI [dcm-]

maeI bfal

asp700

rmaI

tsp5091 apol

apyI[dcm+]

niaIII taqI[dam-]

1301 CATCITIC TATICATGGG ATCGAGGGCG CGTITGATGA GCCTGGAACT AAACAGTCA TACCTGGCCG AGTTATAGGA AAAITITCAA TCCGTCTAGT bst4CI/hpyCH4III alw1[dam-] bsh1236I

GTAGAGAAAG ATAAGTACCC TAGCTCCCGC GCAAACTACT CGGACCTTGA TTTTGTCAGT ATGGACCGGC TCAATATCCT TTTAAAAGTT AGGCAGATCA I E G A 346

[G	E.	권	nlaII	.401 CCCTCACATG ARTGICTUTG OGGIGGAAAA ACAGGIGACA CGACATCTIG AAGAIGIGIT CICCAAAAGA AAIAGIICCA ACAAGAIGGI IGIIICCAIG	IC GCCACCITITI IGTCCACTGI GCTGTAGAAC TICTACACAA GAGGITITCI TIATCAAGGI IGTICTACCA ACAAAGGTAC	A VEK QVT RHLE DVF SKR N SSN KMV VSM
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rmal	dsaI				tseI	1/Iodm	nbol/ndell[dam-]		ďp
maeI	btg1/	btg1/bstDSI sspI	H		fnu4HI/bsoFI	fl dpn[[dam-]	_dam-]		qp
bfaI	bsaJI	bsaJI hpyCH4V		bsrI	bbvI	dpnI[dam+]	lam+]		alw
ACTCTAGGAC	TACACCCGTG	GATTGCAAAT	ATTGATGACA	CCCAGTATCT	ACTOTAGGAC TACACCOGTG GATTGCAAAT ATTGATGACA CCCAGTATOT CGCAGCAAAA AGAGCGATCA GAACAGTGTT TGGAACAGAA CCAGALATGA.	AGAGCGATCA	GAACAGTGTT	TGGAACAGAA	CCAGATATGA.
TGAGATCCTG	ATGTGGGCAC	CTAACGTTTA	TAACTACTGT	GGGTCATAGA	TGAGAICCIG AIGIGGGCAC CIAACGITIA IAACIACIGI GGGICAIAGA GCGICGILIT ICICGCIAGI CIIGICACAA ACCIIGICII GGICIAIACI	rctcgctagt	CTTGTCACAA	ACCTTGTCTT	GGTCTATACT
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mbol/ndeII[dam-] sau3AI

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serFI[dcm-] dpnII[dam-] fokI dpnI[dam+]

sau3AI

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[-mp]liepu/loqu I9dsd

dpnII[dam-] mvaI

ecoRII[dcm-]

alwI[dam-]

ncil

nlaIV

nspl

scrFi[M.hpaII-]

dsaV[dcm-]

bstNI dpnI[dam+]

basKI[dcm-] apyI[dcm+]

mun1/mfeI tsp5091

alwI[dam-]

bssKI

446

bamBI

dsav

bstYI/xhoII

hpaII

aciī. IOMI

aluI

mspA11/nspBII

1601 TOCGGGATGG ATCCACCATT CCAATTGCCA AAATGTTCCA GGAGATCGTC CACAAGAGCG TGGTGCTAAT TCCGCTGGGA GCTGTTGATG ATGGAGAACA AGGCCCTACC TAGGTGGTAA GGTTAACGGT TITACAAGGT CCTCTAGCAG GTGTTCTCGC ACCACGATTA AGGCGACCCT CGACAACTAC TACCTCTTGT G AVD'D ט r L A L I × EIV E4 E3

tru9I

mseI

tseI

nlaIV

sau961[M.haeIII-] fnu4HI/bsoFI

1701 TTCGCAGAAT GAGAAAATCA ACAGGTGGAA CTACATAGAG GGAACCAAAT TATTTGCTGC CTTTTTCTTA GAGATGGCCC AGCTCCATTA ATCACAAGAA 'haeIII/pall aseI/asnI/vspI tsp509I bbvI mnli

AAGCGICTTA CICITITAGI IGICCACCII GAIGIAICIC CCIIGGIIIA AIAAACGACG GAAAAAGAAI CICIACCGGG ICGAGGIAAI IAGIGIICII H H M A O [zi × S

sau3AI

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dpnII[dam-] dpnI[dam+] hpy188I

rmaI mael

> tspRI hpy188I alwI[dam-] sau3AI

bslI hphI mbol/ndeII[dam-]

rmal

fokI fokI bfaI bsli tfir mull dpnII[dam-]

1801 CCTTCTAGIC TGATCTGAIC CACTGACAGA TICACCICCC CCACAICCCI AGACGGGAI GGAAIGTAAA TAICCAGAGA AITIGGGICI AGIAIAGIAC bfaI hpy188III bstF5I bstFSI hinfI[M.hphI-] dpnI[dam+] mael bfaI

GGAAGATCAG ACTAGACTAG GTGACTGTCT AAGTGGAGGG GGTGTAGGGA TCTGTCCCTA CCTTACATTT ATAGGTCTCT TAAACCCAGA TCATATCATG

csp6I

rsaI

maeī rmaI

tsp5091 apoI sau96I

nlaIV

hpyCH4V avall

mbol/ndeil[dam-]

sau3AI

dpnII[dam-] dpnI[dam+]

bsgI eco01091/drall Dindd

tspRI tru9I

btsI msel bsmFI

1901 ATTITCCCTI CCALTIAAAA TGICITGGGA TATCTGGATC AGTAALAAAA TATITCAAAG GCACAGAIGI TGGAAATGGT ITAAGGTCCC CCACTGCACA taaaagggaa ggiaaatitt acagaaccci atagacctag tcattatttt ataaagttic cgtgtctaca acctitacca aattccaggg ggtgacgtgt

sspī

ecoRV alw1[dam-]

ahaIII/draI

tru9I

mseI

hpy188III

scrFI[dcm-]

pspGI

mvaI

ecoRII[dcm-]

dsaV[dcm-]

tseI

cacBI

bstNI

bssKI [dcm-]

tfil apyI[dcm+] Iled. fnu4HI/bsoFI

bbvI

bbvi aluI

Smli

fnu4HI/bsoFI

tseI

2001 CCTTCCTCAA GTCATAGCTG CTTGCAGCAA CTTGATTTCC CCAAGTCCTG TGCAATAGCC CCAGGATTGG ATTCCTTCCA ACCTTTTAGC ATATCTCCAA GGAAGGAGII CAGIAICGAC GAACGICGII GAACIAAAGG GGIICAGGAC ACGIIAICGG GGICCIAACC IAAGGAAGGI IGGAAAAICG IAIAGAGGII hpyCH4V bsaJI hpyCH4V

hinfl

tsp45I sau96I

bassI avaII

eco01091/draII hpy188III hqiAI/aspHI IMudd

**bsp1286** rmaI

Idsm

mbol/ndeIl[dam-] dpnII[dam-] dpnI[dam+]

sau3AI

bsinkal smll mael hpaII

mnlI bfaI

bsaWI

hpyCH4V

bstF5I fokī

bmyl .maeIII

2101 CCTIGCAAIT TGAITGGCAT AATCACICCG GIIIGCIITC IAGGICCICA AGIGCICGIG ACACATAAIC AITCCAICCA AIGAICGECT IIGCIITACC ggaacgttaa actaaccgta ttagtgaggc calacgaaag atccaggagt tcacgagcac tgtgtattag taaggtaggt tactagcgga aacgaaatgg

tru9I

bsmAI mseI

tspRI bsal asel/asnl/vspl

tcagaaagga aaatagaata attatitita caaccagagg tggtgacnga gggttttttt titttittt titttittt titttttt

scrFI[M.hpaII-]

ncil

Idsm

hpall

sau96I rsaI

bssKI

nlaIV rarII/cspI mrol xmaI/pspAI smal kpnI hpyCH4V scrfi[M.hpali-] cpol

aciI

hpy188III csp6I taqI nciI fnu4HI/bsoFI

banI sfcI PspMII sstI salI dsaV haeIII/pall

sacI hincII/hindII[M.taqI-] avaII[M.hpaII-] asp718 eagl/xmall1/eclXI alul acc1[M.taq1-] tru9I mspI ncrl

hgiAI/aspHI[M.alu1-] mseI bspBI cfr10I/bsrFI eaeI

bssKI asel/asnI/vspI acc651 cac81 ec1136II rmaI cfrI

pstI bsp1286[M.aluI-] xmnI tsp509I bsaWI mael bsiEI

sse8387I bsaJI tsp509I bsaWI ageI baleKAI bfaI notI

csp6I aluI banii[M.alui-] asp700 acciii hpali sbfi bmyl hpy991 aval[M.hpall-] hpall mspl bspMI speI fnu4HI/bsoFI acil

rsaI

2301 AAAAAAAA AAAAAAAA AAAGGCGGC CGCCGACTAG TGAGCTCGTC GACCCGGGAA TTAATTCCGG ACCGGTACCT GCAGGCGTAC CAGCTTTCCC TITITITITI ITTITITI TITCCCCCC GCGCTGAIC ACTCGAGCAG CTGGGCCCTT AATTAAGGCC TGGCCATGGA CGTCCCATG GTCGAAAGGG

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2401 TATAGTGAGT CGTATTAGAG CTTGG ATAICACTCA GCATAATCTC GAACC GSeqEdit, DNA92234 [Full], page 15

dsaV

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aatii(GACGTC):	25
acc651 (GGTACC):	1295 2374
accI (GIMKAC):	727 1117 2348
acciii (TCCGGA):	2366
acil(CCGC):	86 332 355 511 1420 1672 2326 2330
acyI (GRCGYC):	. 25
aflii (ACRYGT):	37
ageI (ACCGGT):	2371
ahaII (GRCGYC):	
ahaIII (TTTBAA):	1914
aluI (AGCT):	19 48 110 485 569 1006 1680 1781 2016 2343 2392 2419
alw261 (CAGNNNCTG):	418 523 565
alwi (ggarcnnnn):	270 271 628 785 959 1319 1599 1609 1610 1817 1936
alwni (Cagninctg) :	418 523 565
apal (GGGCCC):	533
apol (RAATTY):	. 54 409 841 1249 1381 1879
apyI (CCMGG):	528 609 813 882 1038 1113 1137 1144 1342 1363 1638 2061
aseI (AITAAT) :	1787 2219 2360
asnI (ATTAAT):	1787 2219 2360
asp700 (Gaannnuttc) :	375 1159 1379 1469 2358
asp718 (GGTACC):	1295 2374
asphi (Gngcwc):	484 2152 2342
asp1 (GachingTC) :	451
aval (CYCGRG):	62 280 995 2353
avali (GGMCC):	559 705 909 1140 1985 2143 2369
ball (TGGCCA):	437
bamHI (GGATCC):	270 1609
banI (GGYRCC):	640 1295 2374
	GSeqEdit, DNA92234 [Full], page 16

banII (GRGCYC):	484 533 809 2342
bbsi (Gaagachnnnnn):	
bbvI (GCAGC):	292 312 315 318 321 508 519 522 567 570 672 1235 1552 1756 2017 2024
bceal (acgconnnnnnnnnn):	502 656
bfar (Crag):	243 1210 1216 1396 1504 1805 1849 1889 2140 2337
bgli (gccnnnnnggc):	535
bglii (agatct):	822
· bmy1 (GDGCHC):	159 484 533 809 2152 2342
bpmI (CTGGAG):	96 258 325 814 883 1290
bpuai (Gaagachinnnni):	130 379 587
bsaAI (YACGTR) :	42
bsafi (GRCGYC):	25
bsai (ggictchnnnn):	1034 2234
bsaji (ccnngg):	139 359 503 528 545 684 812 881 995 996 1143 1516 2060 2353
bsawi (wccegw):	1226 2127 2366 2371
bseri (gaggagnnnnnnnnn) :	342 749 1270
bsgI (GTGCAG):	415 670 1994
bsh1236I (CGCG):	38 331 1329
bsiei (cgrycg):	755 2327
bsifikai (Gwgcwc):	484 2152 2342
bsiwi (cgracg):	40
bsli (ccnnnnnngg):	135 184 274 275 354 396 614 631 771 1847 1848 2060
bsmAI (GTCTC):	1034 2235
bsmal (GTCTC):	1034 2235
Dempi (GGGACNINININININININI):	-
bsofi (GCNGC):	85 292 312 315 318 321 332 508 519 522 567 570 672 1235 1552 1756
	. 2017 2024 2326 2329
bsp1201 (GGGCCC):	533
bsp1286 (GDGCHC):	159 484 533 809 2152 2342
Depchi (CTCAGNNNNNNNNN):	563 1050
	GSeqEdit, DNA92234 [Full], page 17

bspei (TCCGGA):	2366
bsphi (TCATGA):	1074
bspMI (ACCTGC):	7722
bspMII (TCCGGA) :	2366
bsrfi (RCCGGY):	2371
bsrI (ACTGGN):	384 618 1542
bsski (ccngg):	139 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1342
	1363 1602 1638 2061 2353 2354
bassi (crcete) :	2155
bst4c1 (ACNGT):	643 1354 1573
bstapi (gcannnntgc):	. 641
bstDSI (CCRYGG):	. 503 1516
bstF5I (GGATG):	405 606 857 1068 1203 1605 1844 1857 2175
bstnI (CCMGG):	528 609 813 882 1038 1113 1137 1144 1342 1363 1638 2061
batul (cgcg):	38 331 1329
bstxi (ccannnnntgg) :	260 1478
bstxI (RGATCY):	270 822 1609
btgI (CCRYGG):	503 1516
btrI (CACGTC):	<i>L</i> 99
bts1 (GCAGTGNN):	1992
cac81 (GCNNGC):	31 35 303 675 868 975 2020 2381 ·
cfol(GCGC):	330 364 525 800 1328
cfr101 (RCCGGY):	2371
ofrI (YGGCCR):	437 500 611 657 1365 2327
cpol(cegrace):	2368
csp6I (GTAC):	41 387 1296 1897 2375 2387
cspi (cgmccg):	2368
ddel (CINAG):	563 1050 1265 1767
dpnI (GATC):	271 628 786 823 960 1090 1320 1566 1599 1610 1644 1812 1817 1937

draI(TTTAAA):     draII(RGGNCCY):     draIII(CACNNNGTG):     dsaI(CCRYGG):     dsaI(CCRYGG):     dsaV(CCNGG):     dsaV(CCNGG):     eaeI(YGGCCR):     eaeI(YGGCCR):     eaeI(CTCTTCNNNNN):     ecll36II(GAGCTC):     ecllXI(CGGCCG):     cclXI(CGGCCG):     cclXI(CGGCCG):	2183 1914 532 558 768 1984 2142 642 503 1516 139 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1342 1363 1602 1638 2061 2353 2354 437 500 611 657 1365 2327 15 487 862 1100 1177 15 487 862 144 489 804 250 424 474 489 804 396 532 558 768 1984 2142
); GTG); IN); TC);	558 768 1984 2142 1516 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1 1602 1638 2061 2353 2354 500 611 657 1365 2327 87 862 1100 1177 2342 424 474 489 804 558 768 1984 2142
GTG): GTG): TC):	558 768 1984 2142.  1516 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1 1602 1638 2061 2353 2354 500 611 657 1365 2327 87 862 1100 1177 2342 424 474 489 804 558 768 1984 2142
GTG): NN): TC):	1516 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1 1602 1638 2061 2353 2354 500 611 657 1365 2327 87 862 1100 1177 2342 424 474 489 804 558 768 1984 2142
NN): TC):	1516 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1 1602 1638 2061 2353 2354 500 611 657 1365 2327 87 862 1100 1177 2342 424 474 489 804 558 768 1984 2142
NN): TC):	360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 1602 1638 2061 2353 2354 500 611 657 1365 2327 87 862 1100 1177 2342 474 489 804 558 768 1984 2142
NN): TC):	53 1602 1638 2061 2353 2354 7 500 611 657 1365 2327 27 487 862 1100 1177 1 2342 27 27 27 558 768 1984 2142
NN): TC):	7 500 611 657 1365 2327 27 487 862 1100 1177 1 2342 27 9 424 474 489 804 5 558 768 1984 2142
NN): TC):	27 487 862 1100 1177 1 2342 27 3 424 474 489 804 5 558 768 1984 2142 .
	487 862 1100 1177 1 2342 27 3 424 474 489 804 5 558 768 1984 2142
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	27 5 424 474 489 804 5 5 558 768 1984 2142
	) 424 474 489 804 ) ! 558 768 1984 2142
eco57I(CTGAAG):	558 768 1984.2142 ·
econi (ccinnnnagg):	558 768 1984.2142 '
eco01091 (RGGNCCX): 532 558 768 1984.2	
ecori (GAATIC):	
	528 609 813 882 1038 1113 1137 1144 1342 1363 1638 2061
ecorv (Gatatc):	66
	85 292 312 315 318 321 332 508 519 522 567 570 672 1235 1552 1756
2017 2024 2326 2329	7 2024 2326 2329
fnuDII(CGCG): 38 331 1329	331 1329
	405 606 857 1068 1203 1605 1844 1857 2175
gsul (CIGGAG): 96 258 325 814 883	96 258 325 814 883 1290 .
haell (RGCGCY): 363 524 799	524 799
438 501	501 534 543 612 658 769 1366 1776 2328
hgaI (GACGC): 295 420	420
hgiai (GNGCWC):	. 2152 2342
hhaI (GCGC): 330 364.525 800 1328	364.525 800 1328
hinPI (GCGC): 330 364 525 800 13	364 525 800 1328
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hincII (GTYRAC):	2348
hindli (Gryrac):	2348
hinfl (GANTC):	204 451 585 914 1120 1148 1275 1500 1829 2070 2407
hinlI (GRCGYC):	. 25
hpall (CCGG):	139 361 684 996 1227 1239 1602 2128 2354 2367 2372
hphi (GGTGA):	3 181 346 1023 1434 1832
hpy188I (TCNGA):	51 79 252 476 491 582 806 946 1568 1809 1814
hpy188III (TCNNGA):	97 281 402 443 1051 1074 1209 1289 1446 1873 1933 2156 2366
hpy99I (CGWCG) :	27 2347
hpych4111 (Acngt):	643 1354 1573
hpych4IV (acgt):	26 43 149 668
hpych4v (TGCA):	34 416 521 671 1030 1283 1524 1995 2023 2051 2104 2380
kpnI (GGTACC):	1295 2374
ksp6321 (CTCTTCNNNN):	15 487 862 1100 1177
mael (CTAG):	243 1210 1216 1396 1504 1805 1849 1889 2140 2337
maeII(ACGT):	26 43 149 668
maelii (GINAC):	4 180 1435 2158
mbol (GATC):	271 628 786 823 960 1090 1320 1566 1599 1610 1644 1812 1817 1937
•	2183
mboli(GAAGA):	15 131 380 488 588 825 862 917 1101 1177 1219 1450
mcrI (CGRYCG):	755 2327
mfel (Caattg):	1622
mluI (ACGCGT):	
mlyi (Gagtonnnn):	204 451 585 1120 1500 2407
mnl1 (ccrc):	65 77 126 185 209 227 246 344 350 396 469 545 562 598 724 749 853
	865 886 1021 1168 1180 1270 1287 1293 1324 1402 1738 1835 2005 214
mrol (TCCGGA):	2366
mscI (TGGCCA):	437
msel(TTAA):	175 1788 1915 1981 2220 2361
msli(Caynnnrrg):	400 1405 1407
	GSeqEdit, DNA92234 [Full], page 20

mspall(CMGCKG):	568 1672
mspi(ccee):	139 361 684 996 1227 1239 1602 2128 2354 2367 2372
muni (CAATTG):	1622
mval (CCWGG):	528 609 813 882 1038 1113 1137 1144 1342 1363 1638 2061
mvnI (CGCG):	38 331 1329
mwoi (gcnnnnnngc):	303 312 315 321 357 502 535 641 650 793 802 1555 1665
ncil (CCSGG):	139 360 684 995 996 1239 1602 2353 2354
ndeII(GATC):	271 628 786 823 960 1090 1320 1566 1599 1610 1644 1812 1817 1937
	2183
nlaili (CATG):	32 199 336 555 1014 1075 1315 1407 1497
nlaIV (GGNNCC):	270 532 533 558 640 705 991 1054 1140 1164 1295 1609 1741 1985 2374
not1(GCGGCCGC):	2326
nspbii (cmgckg):	568 1672
nsphi (RCATGY):	31 335
nspi (RCAIGY):	31 335
paer/i (crcgg):	
pall(GGCC):	438 501 534 543 612 658 769 1366 1776 2328
pflf1 (GachingTC) :	451
plei (Gagtchnn):	204 451 585 1120 1500 2407
ppumi (regrecy):	558 1984 2142
pshai (Gachningic) :	553
pspal (CCCGGG):	995 2353
pspGI (CCWGG):	528 609 813 882 1038 1113 1137 1144 1342 1363 1638 2061
pspomi (gegccc):	533
pst1 (crecag):	520 2379
pruli (Cagcig) :	268
rcal (TCATGA):	1074
rmal (CTAG):	243 1210 1216 1396 1504 1805 1849 1889 2140 2337
rsaI (GTAC):	41 387 1296 1897 2375 2387
rsii (cggmccg):	2368
	GSeqEdit, DNA92234 [Full], page 21

	CGAC): 2348	:CTICUNNN):	(GAIC): 271 628 786 823 960 1090 1320 1566 1599 1610 1644 1812 1817 1937	2183	(GGNCC):	2378 236CAGG):	139 360 528 609 684	1363 1602 1638 2061 2353 2354		TRYAG): 10 520 2379 2400	GCCNNINNGGCC):	CCGGG):	TYRAG): 62 2006 2147	TACGTA):	CTAGT): 2336	CANGC):	STACG):	71 (CCTGCAGG):	ATATT):	AGCTC):	CGT):	55A):	NWTC):	38 331 1329	rcaig):	TAA):	WGC):	GTSAC): 4 180 1435 2158 .	(AATT): 55 410 842 942 1250 1382 1663 1748 1880 2107 2359 2363	sall(GTCGAC):  sau3Al(GATCTTCNNNN):  sau3Al(GATC):  sau3Al(GATC):  sau96I(GGRCC):  spin(CCTCCAGG):  sfil(GCATC):  sfil(GGCCNNNNGGCC):  spin(CCTRAGT):  spin(CTRAGT):  spin(CTRAGT):  spin(GCATC):  spin(GCATGC):  spin(G	2346 15 486 1099 271 628 786 823 960 1090 1320 1566 1599 1610 1644 1812 1817 1937 2183 253 534 559 705 769 909 1140 1776 1985 2143 2369 2378 139 360 528 609 684 813 882 995 996 1038 1113 1137 1144 1239 134 1363 1602 1638 2061 2353 2354 10 520 2379 2400 10 520 2379 2400 10 520 2379 2400 11 520 2379 2400 12 52 2006 2147 12 11 11 11 11 11 11 11 11 11 11 11 11 1
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tepri (nncagignn) ;	1574 1821 1992 2243
tth1111 (GACNNNGTC):	451
vspI (AITAAI):	1787 2219 2360
xbaI (TCTAGA):	1209
xhoI (CTCGAG):	62
xholl (RGATCY):	270 822 1609
xmaI (CCCGGG):	995 2353
xmaIII (CGGCCG):	2327
xmil (GAANNNITC):	375 1150 1370 1460 2350

## t found:

eco72I (CACGTG), eco81I (CCTWAGG), ehel (GGCGCC), esp3I (CGTCTC), espI (GCTWAGC), fseI (GGCCGGCC), fspI (TGCGCA), hindIII (AAGCTT) osu36I (CCINAGG), celli (GCINAGC), clai (ATCGAI), drdi (GACNNNNNGTC), eaml105I (GACNNNNGTC), ecii (GGCGGA), eco47111 (AGCGCI). pmel (GITIABAC), pmli (CACGIG), ppul 01 (AIGCAI), psil (TIATAA), pspl 4061 (AACGII), pvul (CGATCG), sacli (CCGCGG), sanDl (GGGWCCC) adel (CAIAIG), ngoMI (GCCGGC), nheI (GCTAGC), nrul (TCGCGA), nsil (AIGCAI), pacl (TIAATTAA), pcil (ACAIGT), pflMI (CCANNNNNIGG) saul (CCINAGG), scal (AGTACT), scel (TAGGGATAACAGGGTAAT), sexAl (ACCWGGT), sful (TTCGAA), sgfl (GCGATCGC), sgrAl (CRCCGGYG) pal (GTTAAC), kasi (GGCGCC), kspi (CCGCGG), mami (GAINNNAIC), mstii (CCINAGG), naei (GCCGGC), nari (GGCGCC), ncoi (CCAIGG), osrDI (GCAATGNN), bsrGI (TGTACA), bssBII (GCGCGC), bst11071 (GTATAC), bstBI (TTCGAA), bstEII (GGTNACC), bst2171 (GTATAC), bembi (cetctcnnnnn), bemi (gaatgcn), bep106 (atcgat), bep14071 (tgtaca), bepci (cgatcg), bepdi (atcgat), berbi (gaccgg), acli (Aacstr), afei (Agcgcr), afili (Ctraag), ahdi (Gacnnnngtc), alw441 (Grgcac), apali (Grgcac), asci (Gccccgcc), avalli (Algcal), avili (Igcgca), avrii (Cctagg), baei (nnnnnnnnnnnnnnngtaychnnnnnnnnn), bbrpi (Cacgtg), nol (GTGCAC), snol (GTGCAC), srfl (GCCCGGGC), sstll (CCGCGG), stul (AGGCCT), styl (CCMWGG), swal (ATTTAAAT), **EXHIBIT B** 

# Find o New o Update

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Assay Neme Mouse Messenglal Cell profferation Assay

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Result Interpretation Any PIN that gives an ebsorptiance reading which is 15% above the media control is considered a hit.

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Date Entered Date Canceled

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Scientist James (Greches) Par Nombrook 0. Assoyers

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